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NEWS	4	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	5	MAR 02	GBFULL: New full-text patent database on STN
NEWS	6	MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced
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NEWS	9	MAR 22	Original IDE display format returns to REGISTRY/ZREGISTRY
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NEWS	16	APR 28	Improved searching of U.S. Patent Classifications for U.S. patent records in CA/CAplus
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FILE 'BIOTECHNO' ENTERED AT 14:40:06 ON 02 AUG 2005

FILE 'CONFSCI' ENTERED AT 14:40:06 ON 02 AUG 2005

FILE 'HEALSAFE' ENTERED AT 14:40:06 ON 02 AUG 2005

FILE 'IMSDRUGCONF' ENTERED AT 14:40:06 ON 02 AUG 2005

FILE 'LIFESCI' ENTERED AT 14:40:06 ON 02 AUG 2005

FILE 'PASCAL' ENTERED AT 14:40:06 ON 02 AUG 2005

=> PTH and antibody and N-terminal

L1	0	FILE AGRICOLA
L2	26	FILE BIOTECHNO
L3	0	FILE CONFSCI
L4	0	FILE HEALSAFE
L5	0	FILE IMSDRUGCONF
L6	8	FILE LIFESCI
L7	13	FILE PASCAL

TOTAL FOR ALL FILES
L8 47 PTH AND ANTIBODY AND N-TERMINAL

=> l8 and non-PTH
L9 0 FILE AGRICOLA
L10 1 FILE BIOTECHNO
L11 0 FILE CONFSCI
L12 0 FILE HEALSAFE
L13 0 FILE IMSDRUGCONF
L14 0 FILE LIFESCI
L15 0 FILE PASCAL

TOTAL FOR ALL FILES
L16 1 L8 AND NON-PTH

=> d l16 ibib abs total

L16 ANSWER 1 OF 1 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1991:21310522 BIOTECHNO
TITLE: Parathyroid hormone-related protein: Biochemistry and molecular biology
AUTHOR: Martin T.J.; Moseley J.M.; Gillespie M.T.
CORPORATE SOURCE: Department of Medicine, University of Melbourne, and St. Vincent's Institute of Medical Research, St. Vincent's Hospital, Fitzroy, Vic. 3065, Australia.
SOURCE: Critical Reviews in Biochemistry and Molecular Biology, (1991), 26/3-4 (377-395)
CODEN: CRBBEJ ISSN: 1040-9238
DOCUMENT TYPE: Journal; General Review
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1991:21310522 BIOTECHNO
AB This article critically reviews the current state of knowledge regarding the recently identified and cloned novel hormone parathyroid hormone-related protein (PTHrP). PTHrP is produced by tumors associated with the syndrome of humoral hypercalcemia of malignancy giving rise to the parathyroid hormone (**PTH**)-like symptoms characteristic of the syndrome. Areas that will be reviewed include identification, purification and cloning, localization, actions, and significance of PTHrP in cancers and normal physiology. The structure and regulation of the PTHrP gene that may be ancestrally related to the **PTH** gene will also be discussed. Studies in vivo and in vitro with synthetic and recombinant PTHrP sequences and **antibodies** developed against them have established that the **PTH**-like actions of PTHrP are mediated via the **N-terminal** sequences, which show some limited sequence homology with **PTH**. Evidence for **PTH** and **non-PTH**-like actions of PTHrP in normal physiology, which implicate a role for PTHrP in fetal and neonatal development, is also presented.

=> dup rem
ENTER L# LIST OR (END):l8
DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF'.
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PROCESSING COMPLETED FOR L8
L17 35 DUP REM L8 (12 DUPLICATES REMOVED)

=> dup rem
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L1 HAS NO ANSWERS

L3 HAS NO ANSWERS
L4 HAS NO ANSWERS
L5 HAS NO ANSWERS
DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L1
PROCESSING COMPLETED FOR L2
PROCESSING COMPLETED FOR L3
PROCESSING COMPLETED FOR L4
PROCESSING COMPLETED FOR L5
PROCESSING COMPLETED FOR L6
L18 29 DUP REM L1-L6 (5 DUPLICATES REMOVED)

=> d l18 ibib abs total

L18 ANSWER 1 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
DUPLICATE
ACCESSION NUMBER: 2003:36899324 BIOTECHNO
TITLE: Functional type I **PTH**/PTHrP receptor in freshly isolated newborn rat keratinocytes: Identification by RT-PCR and immunohistochemistry
AUTHOR: Errazahi A.; Bouizar Z.; Lieberherr M.; Souil E.; Rizk-Rabin M.
CORPORATE SOURCE: Dr. M. Rizk-Rabin, CNRS UPR 1524, Hopital Saint Vincent de Paul, 82 Avenue Denfert Rochereau, 75014 Paris, France.
E-mail: rizk-rabin@cochin.inserm.fr
SOURCE: Journal of Bone and Mineral Research, (01 APR 2003), 18/4 (737-750), 40 reference(s)
CODEN: JBMREJ ISSN: 0884-0431
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:36899324 BIOTECHNO
AB The presence of identical or distinct type I parathyroid hormone (**PTH**)/parathyroid hormone - related peptide (PTHrP) receptors in keratinocytes is still a matter of debate. We studied the expression and functionality of PTHrP receptors in freshly isolated keratinocytes from newborn rat skin. Four overlapping primers, amplifying different regions in the rat **PTH** receptor, were used for reverse transcriptase-polymerase chain reaction (RT-PCR). The first region corresponded to the **N-terminal** extracellular region and the first transmembrane domain (S/M1), the second region amplified the connecting intracellular and extracellular loops transmembrane domain (E2/M5), the third spanned the range from the transmembrane to the intracellular domain (M4/T), and the fourth region amplified the C-terminal tail (M6/7/T). The PCR products from the keratinocyte RNA were identical to those from kidney RNA of the same rats. The cloned four transcripts showed 100% of homologies with the cDNA sequence from bone ROS cells. Keratinocytes, freshly isolated or present in situ in the epidermis, recognized an anti-**PTH** receptor **antibody** (**PTH**-II) directed against the receptor extracellular domain. Western blotting showed the same protein patterns in keratinocytes, kidney, and ROS cell extracts. Low doses of PTHrP(1-34) (10.sup.-.sup.1.sup.2-10.sup.-.sup.9 M) increased the cell number studied by [.sup.3H]thymidine incorporation and DNA content. Treatment with the **PTH**/PTHrP receptor antagonist [Asn.sup.1.sup.0, Leu.sup.1.sup.1, D Trp.sup.1.sup.2] PTHrP(7-34) or two different **PTH** receptor **antibodies** inhibited the increase in cell proliferation induced by PTHrP(1-34). All these findings indicate that newborn rat epidermis and keratinocytes express functional PTHrP receptors, which are identical to type I **PTH**/PTHrP receptor and are recognized by PTHrP(1-34).

L18 ANSWER 2 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2002:34968982 BIOTECHNO
TITLE: Purification and characterization of a receptor for human parathyroid hormone and parathyroid hormone-related peptide
AUTHOR: Shimada M.; Chen X.; Cvrk T.; Hilfiker H.; Parfenova M.; Segre G.V.
CORPORATE SOURCE: G.V. Segre, Endocrine Unit, Wellman 501, Massachusetts General Hospital, Boston, MA 02114, United States. E-mail: segre@helix.mgh.harvard.edu
SOURCE: Journal of Biological Chemistry, (30 AUG 2002), 277/35 (31774-31780), 89 reference(s)
CODEN: JBCHA3 ISSN: 0021-9258
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2002:34968982 BIOTECHNO
AB The human parathyroid hormone (**PTH**) receptor (hPTH1R), containing a 9-amino acid sequence of rhodopsin at its C terminus, was transiently expressed in COS-7 cells and solubilized with 0.25% n-dodecyl maltoside. Approximately 18μg of hPTH1R were purified to homogeneity per mg of crude membranes by single-step affinity chromatography using 1D4, a monoclonal **antibody** to a rhodopsin epitope. The N terminus of the hPTH1R is Tyra.sup.2.sup.3, consistent with removal of the 22-amino acid signal peptide. Comparisons of hPTH1R by quantitative immunoblotting and Scatchard analysis revealed that 75% of the receptors in membrane preparations were functional; there was little, if any, loss of functional receptors during purification. The binding affinity of the purified hPTH1R was slightly lower than membrane-embedded hPTH1R (K.sub.d = 16.5 ± 1.3 versus 11.9 ± 1.9 nM), and the purified receptors bound rat [Nle.sup.8.sup.,.sup.2.sup.1,Tyr.sup.3.sup.4]**PTH**-(1-34)-NH.sub.2 (**PTH**-(1-34)), and rat [Ile.sup.5,Trp.sup.2.sup.3,Tyr.sup.3.sup.6]PTHrP-(5-36)- NH.sub.2 with indistinguishable affinity. Maximal displacement of .sup.1.sup.2.sup.5I-**PTH**-(1-34) binding by rat [α-aminoisobutyric acid (Aib) .sup.1.sup...sup.3,Nle.sup.8,Gln.sup.1.sup.0,Har.sup.1.sup.1, Ala.sup.1.sup.2,Trp.sup.1.sup.4,Arg.sup.1.sup.9,Tyr.sup.2.sup.1]. **PTH**-(1-21)-NH.sub.2 and rat [Aib.sup.1.sup.,.sup.3,Gln.sup.1.sup.0,Har.sup.1.sup.1,Ala.sup.1.sup.2, Trp.sup.1.sup.4]**PTH**-(1-14)-NH.sub.2 of 80 and 10%, respectively, indicates that both **N-terminal** and juxtamembrane ligand binding determinants are functional in the purified hPTH1R. Finally, **PTH** stimulated [.sup.3.sup.5S]GTPγS incorporation into Gα.sub.s in a time- and dose-dependent manner, when recombinant hPTHiR, Gα.sub.s-, and βγ-subunits were reconstituted in phospholipid vesicles. The methods described will enable structural studies of the hPTH1R, and they provide an efficient and general technique to purify proteins, particularly those of the class II G protein-coupled receptor family.

L18 ANSWER 3 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
DUPLICATE
ACCESSION NUMBER: 2002:34966763 BIOTECHNO
TITLE: Both N- and C-terminal domains of parathyroid hormone-related protein increase interleukin-6 by nuclear factor-κB activation in osteoblastic cells
AUTHOR: Guillen C.; Martinez P.; De Gortazar A.R.; Martinez M.E.; Esbrit P.
CORPORATE SOURCE: P. Esbrit, Mineral Metabolism Laboratory, Research Unit, Fundacion Jimenez Diaz, Avda. Reyes Catolicos 2,

28040 Madrid, Spain.
E-mail: pesbrit@fjd.es
SOURCE: Journal of Biological Chemistry, (02 AUG 2002), 277/31 (28109-28117), 53 reference(s)
CODEN: JBCHA3 ISSN: 0021-9258
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2002:34966763 BIOTECHNO
AB Parathyroid hormone (**PTH**)-related protein (PTHrP) seems to affect bone resorption by interaction with bone cytokines, among them interleukin-6 (IL-6). Recent studies suggest that nuclear factor (NF)-κB activation has an important role in bone resorption. We assessed whether the **N-terminal** fragment of PTHrP, and its C-terminal region, unrelated to **PTH**, can activate NF-κB, and its relationship with IL-6 gene induction in different rat and human osteoblastic cell preparations. Here we present molecular data demonstrating that both PTHrP (1-36) and PTHrP (107-139) activate NF-κB, leading to an increase in IL-6 mRNA, in these cells. Using anti-p65 and anti-p50 **antibodies**, we detected the presence of both proteins in the activated NF-κB complex. This effect induced by either the N- or C-terminal PTHrP domain in osteoblastic cells appears to occur by different intracellular mechanisms, involving protein kinase A or intracellular Ca.sup.2.sup.+/protein kinase C activation, respectively. However, the effect of each peptide alone did not increase further when added together. Our findings lend support to the hypothesis that the C-terminal domain of PTHrP, in a manner similar to its **N-terminal** fragment, might stimulate bone resorption. These studies also provide further insights into the putative role of PTHrP as a modulator of bone remodeling.

L18 ANSWER 4 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN DUPLICATE
ACCESSION NUMBER: 2001:32230589 BIOTECHNO
TITLE: Development of a novel immunoradiometric assay exclusively for biologically active whole parathyroid hormone 1-84: Implications for improvement of accurate assessment of parathyroid function
AUTHOR: Gao P.; Scheibel S.; D'Amour P.; John M.R.; Rao S.D.; Schmidt-Gayk H.; Cantor T.L.
CORPORATE SOURCE: Dr. P. Gao, Department of R and D, Scantibodies Laboratory, Inc., 9336 Abraham Way, Santee, CA 92071, United States.
SOURCE: Journal of Bone and Mineral Research, (2001), 16/4 (605-614), 27 reference(s)
CODEN: JBMREJ ISSN: 0884-0431
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2001:32230589 BIOTECHNO
AB We developed a novel immunoradiometric assay (IRMA; whole parathyroid hormone [**PTH**] IRMA) for **PTH**, which specifically measures biologically active whole **PTH**(1-84). The assay is based on a solid phase coated with anti-**PTH**(39-84) **antibody**, a tracer of .sup.1.sup.2.sup.5I-labeled **antibody** with a unique specificity to the first **N-terminal** amino acid of **PTH**(1-84), and calibrators of diluted synthetic **PTH**(1-84). In contrast to the Nichols intact **PTH** IRMA, this new assay does not detect **PTH**(7-84) fragments and only detects one immunoreactive peak in chromatographically fractionated patient samples. The assay was shown to have an analytical

sensitivity of 1.0 pg/ml with a linear measurement range up to 2300 pg/ml. With this assay, we further identified that the previously described non-(1-84)**PTH** fragments are aminoterminally truncated with similar hydrophobicity as **PTH**(7-84), and these **PTH** fragments are present not only in patients with secondary hyperparathyroidism (2°-HPT) of uremia, but also in patients with primary hyperparathyroidism (1°-HPT) and normal persons. The plasma normal range of the whole **PTH**(1-84) was 7-36 pg/ml (mean ± SD: 22.7 ± 7.2 pg/ml, n = 135), whereas over 93.9% (155/165) of patients with 1°-HPT had whole **PTH**(1-84) values above the normal cut-off. The percentage of biologically active whole **PTH**(1-84) (pB%) in the pool of total immunoreactive "intact" **PTH** is higher in the normal population (median: 67.3%; SD: 15.8%; n = 56) than in uremic patients (median: 53.8%; SD: 15.5%; n = 318; p < 0.001), although the whole **PTH**(1-84) values from uremic patients displayed a more significant heterogeneous distribution when compared with that of 1°-HPT patients and normals. Moreover, the pB% displayed a nearly Gaussian distribution pattern from 20% to over 90% in patients with either 1°-HPT or uremia. The specificity of this newly developed whole **PTH**(1-84) IRMA is the assurance, for the first time, of being able to measure only the biologically active whole **PTH**(1-84) without cross-reaction to the high concentrations of the aminoterminally truncated **PTH** fragments found in both normal subjects and patients. Because of the significant variations of pB% in patients, it is necessary to use the whole **PTH** assay to determine biologically active **PTH** levels clinically and, thus, to avoid overestimating the concentration of the true biologically active hormone. This new assay could provide a more meaningful standardization of future **PTH** measurements with improved accuracy in the clinical assessment of parathyroid function.

L18 ANSWER 5 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2001:32977265 BIOTECHNO
TITLE: A prospective, longitudinal study of the long-term effect of treatment on bone density in children with celiac disease
AUTHOR: Mora S.; Barera G.; Beccio S.; Menni L.; Proverbio M.C.; Bianchi C.; Chiumello G.
CORPORATE SOURCE: Dr. S. Mora, Laboratory of Pediatric Endocrinol., H San Raffaele, Via Olgettina 60, 20132 Milano MI, Italy.
SOURCE: Journal of Pediatrics, (2001), 139/4 (516-521), 22 reference(s)
CODEN: JOPDAB ISSN: 0022-3476
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2001:32977265 BIOTECHNO
AB Objective: Because osteopenia is a frequent complication of celiac disease, we evaluated the impact of a long-term gluten-free diet (GFD), initiated during childhood, on bone density. Study design: Patients with celiac disease (n = 19; mean age, 14.2 ± 2.6 years) were studied after 4.3 ± 0.6 years of GFD. Bone density had been measured at diagnosis and after 1 year of GFD. We also studied 211 healthy children as a control group. Bone mineral density was measured by dual-energy x-ray absorptiometry. Intact parathyroid hormone (**PTH**) and bone-specific alkaline phosphatase (BALP) levels were measured in serum, and **N-terminal** telopeptide of type I collagen (NTx) was measured in urine. Results: Although at diagnosis bone mineral content, bone area, and bone mineral density were significantly lower than in control subjects, the 3 measurements were normal after GFD. None of the patients on a GFD showed elevated values of **PTH**.

Patients on a GFD had BALP (110.2 ± 67.2 U/L) and NTx levels (261.9 ± 187.8 nmol bone collagen equivalents/mmol creatinine) that were significantly higher than those of control subjects. The levels of BALP and NTx were significantly higher in patients with good compliance with the GFD, compared with patients with poorer compliance. Conclusions: This study shows that bone mineral content, bone area, and bone mineral density improve significantly with a GFD.

L18 ANSWER 6 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2000:30799457 BIOTECHNO
TITLE: Processing of chromogranin A in the parathyroid: Generation of parastatin-related peptides
AUTHOR: Fasciotto B.H.; Denny J.C.; Greeket G.H. Jr.; Cohn D.V.
CORPORATE SOURCE: D.V. Cohn, Department Molecular Biology, Health Sciences Center, University of Louisville, Louisville, KY 40292, United States.
E-mail: dvcohn@louisville.edu
SOURCE: Peptides, (2000), 21/9 (1389-1401), 54 reference(s)
CODEN: PEPTDO ISSN: 0196-9781
PUBLISHER ITEM IDENT.: S0196978100002837
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2000:30799457 BIOTECHNO
AB Chromogranin A (CgA) is a glycoprotein present in secretory granules of endocrine cells. In the parathyroid, it is costored and cosecreted with parathormone (**PTH**) in response to hypocalcemia. CgA is the precursor of several bioactive peptides including pancreastatin and betagranin. Parastatin (PARA, pCgA.sub.3.sub.4.sub.7.sub.-.sub.4.sub.1.sub.9) is a novel peptide that we generated in vitro by enzymatic digestion of pCgA. In vitro, it inhibits low Ca.sup.2.sup.+-stimulated parathyroid secretion. Full activity resides in its first 19 residues. In order to determine if PARA or PARA-derived peptides are natural products of the parathyroid, we generated an antiserum directed against pCgA.sub.3.sub.4.sub.7.sub.-.sub.3.sub.5.sub.9 corresponding to the bioactive **N-terminal** sequence of pPARA (pPARA.sub.1.sub.-.sub.1.sub.3 antiserum), and developed a specific radioimmunoassay that we used in conjunction with various chromatographic separations. We identified small peptides carrying the pPARA.sub.1.sub.-.sub.1.sub.3 immunoactivity in extracts and secretion medium of porcine parathyroid glands. Continuous and pulse-chase radiolabeling studies, along with immunoprecipitation using PARA.sub.1.sub.-.sub.1.sub.3 antiserum demonstrate that a newly-synthesized PARA-related peptide fraction with a Mr of 11 kDa is secreted by the parathyroid cells and accumulates in the secretion medium. Edman degradation of the 11 kDa PARA-related peptide band by Edman degradation yielded three major **N-terminal** sequences: S-K-M-D-R-L-A-K-E-L-(residues 313-322), D-R-L-A-K-E-L-T-A-E-(residues 316-325), and A-K-E-L-T-A-E-K-R-L-(residues 319-329), in a molar ratio of approximately 1:2:1. The peptide bonds required to be cleaved to yield these peptides, Trp-Ser, Met-Asp and Leu-Ala, suggest that a chymotrypsin-like endopeptidase participated in their formation. The molecular size and the results of amino acid compositional analysis, indicate that the C-termini of these peptides extended variably to residues 384-401 of pCgA. These results demonstrate that processing of CgA by the parathyroid gland generates bioactive PARA-related peptides that could affect the gland's secretory activity. Copyright (C) 2000 Elsevier Science Inc.

L18 ANSWER 7 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2000:30367938 BIOTECHNO

TITLE: C-terminal parathyroid hormone-related protein increases vascular endothelial growth factor in human osteoblastic cells

AUTHOR: Esbrit P.; Alvarez-Arroyo M.V.; De Miguel F.; Martin O.; Martinez M.E.; Caramelo C.

CORPORATE SOURCE: Dr. C. Caramelo, Laboratorio de Nefrologia, Fundacion Jimenez Diaz, Avda. Reyes Catolicos 2, 28040 Madrid, Spain.
E-mail: ccaramelo@fjd.es

SOURCE: Journal of the American Society of Nephrology, (2000), 11/6 (1085-1092), 52 reference(s)
CODEN: JASNEU ISSN: 1046-6673

DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AN 2000:30367938 BIOTECHNO

AB The **N-terminal** region of parathyroid hormone (**PTH**) and **PTH**-related protein (PTHrP) interacts with a common **PTH**/PTHrP receptor in osteoblasts. These cells synthesize PTHrP, but its role in bone turnover is unclear. Intermittent treatment with **N-terminal** PTHrP or **PTH** stimulates bone growth in vivo, possibly by increasing local bone factors. In addition, C-terminal PTHrP (107-139), which does not bind to the **PTH**/PTHrP receptor, appears to affect bone resorption in vivo and in vitro, although its effect on bone formation in vivo remains controversial. Bone angiogenesis is an often overlooked but critical event in the process of bone remodeling. Recently, **PTH** (1-34) has been shown to induce gene expression of vascular endothelial growth factor (VEGF), a potent angiogenic factor, by osteoblastic cells. However, no data are available on the effect of PTHrP (107-139) on VEGF expression in these cells. Using semiquantitative reverse transcription followed by PCR, we found that PTHrP (107-139), between 10 nM and 1 pM, increased VEGF mRNA in human osteoblastic (hOB) cells from trabecular bone. This effect of this agonist, at 10 nM, was maximal (fivefold for VEGF.sub.1.sub.6.sub.5, and twofold for VEGF.sub.1.sub.2.sub.1 compared to control) within 1 to 4 h. This effect was similar to that induced by PTHrP (1-34) in these cells, as well as in human osteosarcoma MG-63 cells, using Northern blot analysis. Moreover, the effect of both peptides, added together at 100 pM, was not higher than that observed with each peptide alone in hOB cells. The effects of PTHrP(107-39) and that of PTHrP (1-34) were abolished by actinomycin D in hOB cells. In these cells, the protein kinase C inhibitor staurosporine, but not the protein kinase A inhibitor H89, inhibited the increase in VEGF mRNA induced by 10 nM PTHrP (107-139). PTHrP (107-139), at 10 nM, also stimulated cytosolic VEGF immunostaining in hOB cells, and VEGF secretion into the medium conditioned by hOB or MG-63 cells for 24 h, which was (ng/mg protein): 10 ± 1 or 5 ± 3 (control), respectively, and 21 ± 1 or 11 ± 2 (PTHrP [107-139]-stimulated), respectively. Furthermore, medium conditioned by these cells for 24 h in the presence of 10 nM PTHrP (107-139), with or without 10 nM PTHrP (1-34), increased about 30% bovine aortic endothelial cell (BAEC) growth at 48 h. This effect was inhibited by adding a specific anti-VEGF **antibody** to the BAEC incubation medium. These findings demonstrate that the C-terminal domain of PTHrP induces expression and secretion of VEGF, a main angiogenic factor, in hOB cells and MG-63 cells. This relationship between PTHrP and VEGF has potential implications for both bone vascularization and bone formation, and neoangiogenesis in PTHrP-producing tumors.

L18 ANSWER 8 OF 29 BIOTECHNO
ACCESSION NUMBER: 1999:30033735 BIOTECHNO
TITLE: Parathyroid hormone-related peptide stimulates DNA

synthesis and insulin secretion in pancreatic islets
AUTHOR: Villanueva-Penacarrillo M.L.; Cancelas J.; De Miguel F.; Redondo A.; Valin A.; Valverde I.; Esbrit P.
CORPORATE SOURCE: P. Esbrit, Lab. of Bone and Mineral Research, Fundacion Jimenez Diaz, Avda. Reyes Catolicos, 2, 28040 Madrid, Spain.
E-mail: pesbrit@fjd.es
SOURCE: Journal of Endocrinology, (1999), 163/3 (403-408), 33 reference(s)
CODEN: JOENAK ISSN: 0022-0795
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1999:30033735 BIOTECHNO
AB Parathyroid hormone (**PTH**)-related protein (PTHrP) is present in the pancreatic islet. Recent data in transgenic mice suggest that PTHrP might modulate islet mass and insulin secretion. In the present study, we assessed the effect of the **N-terminal PTH** -like region of PTHrP on DNA synthesis in isolated rat islets. PTHrP (1-34), between 1 pM and 10 nM, for 48 h stimulated [.sup.3H]thymidine incorporation into rat islets. This effect was maximally induced, about 2.5-fold over control, by 10 pM of this peptide, decreasing thereafter. In contrast, PTHrP (38-64) amide or PTHrP (107-139) were ineffective in increasing DNA synthesis in islets. Using reverse transcription followed by PCR, we confirmed that rat islets express PTHrP and the type I **PTH**/PTHrP receptor. Addition of a neutralizing anti-PTHrP **antibody** to the incubation medium of proliferating islets decreased islet DNA synthesis by 30%. The effect of a submaximal dose (30 pM) of PTHrP (1-34) on DNA synthesis in rat islets was abolished by 25 nM bisindolylmaleimide I, a protein kinase C (PKC) inhibitor, but not by 25 μM adenosine 3',5'-cyclic monophosphorothioate, Rp-isomer, a protein kinase A inhibitor. Moreover, 100nM phorbol-12-myristate-13-acetate for 48 h also increased DNA synthesis 2-fold over controls in islets. PTHrP (1-34), at 100 nM, in contrast to 50 μM forskolin or 10 mM NaF, failed to affect adenylate cyclase activity in islet membranes. PTHrP, at 30 pM, was also found to increase 2-fold insulin released into the islet-conditioned medium within 24-48 h. Our results suggest that PTHrP is a modulator of pancreatic islet growth and/or function by a PKC-mediated mechanism.

L18 ANSWER 9 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1998:29002064 BIOTECHNO
TITLE: Development of a scintillation proximity assay for high-throughput measurement of intact parathyroid hormone
AUTHOR: Frolik C.A.; Black E.C.; Chandrasekhar S.; Adrian M.D.
CORPORATE SOURCE: C.A. Frolik, Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN 46285, United States.
SOURCE: Analytical Biochemistry, (15 DEC 1998), 265/2 (216-224), 31 reference(s)
CODEN: ANBCA2 ISSN: 0003-2697
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1998:29002064 BIOTECHNO
AB A simple, high-throughput scintillation proximity assay (SPA) for parathyroid hormone (1-84) (**PTH**) has been developed. Fifteen commercially available **N-terminal** and six C-terminal anti-**PTH antibodies** were evaluated for detection of human **PTH**(1-84). Two C-terminal **antibodies** (CR1073M

and 10- P55) gave the most consistent results. Using one of these **antibodies** (10- P55), an assay was developed with a sensitivity of 4 pg/ml for human and rat **PTH**(1-84). Porcine **PTH** (1-84) was not detectable. The intra-assay and inter- assay coefficients of variation for a 467 pg/ml sample were 6.1 and 6.5%, respectively, and for a 21 pg/ml sample, 6.2 and 4.4%. Human **PTH**(1-34), while not detected in the assay, interfered with the detection of **PTH** (1-84). Smaller fragments ¢for example, human **PTH**(3-34)! and a C-terminal **PTH** fragment ¢**PTH**(53-84)! did not interfere in the assay. The procedure gave 106- 110% recovery of human **PTH**(1-84) spiked into samples. Immunoreactive **PTH** concentrations in serum of rats administered EGTA were determined by SPA and by a commercially available **PTH** immunoassay. There was a good correlation between the two assays with significant increases in serum immunoreactive **PTH** concentrations at 15 and 30 min after EGTA injection and a rapid decrease to baseline values by 60 min. The SPA gives a high-throughput method for simply and accurately determining **PTH**(1-84) concentrations in serum.

L18 ANSWER 10 OF 29 LIFESCI COPYRIGHT 2005 CSA on STN
ACCESSION NUMBER: 1998:94463 LIFESCI
TITLE: Expression of alternatively spliced isoforms of the parathyroid hormone (**PTH**)/**PTH**-related peptide receptor messenger RNA in human kidney and bone cells
AUTHOR: Jobert, A.-S.; Fernandes, I.; Turner, G.; Coureau, C.; Prie, D.; Nissenson, R.A.; Friedlander, G.; Silve, C.
CORPORATE SOURCE: INSERM U 426, Faculte de Medecine Xavier Bichat and IFR "Cellules Epitheliales," 16 rue Henri Huchard, BP 416 75870 Paris cedex 18, France
SOURCE: MOL. ENDOCRINOL., (19970900) vol. 10, no. 9, pp. 1066-1076. ISSN: 0888-8809.
DOCUMENT TYPE: Journal
FILE SEGMENT: N; T
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Using a PCR-based strategy, two variants of the **PTH/PTH** -related peptide (**PTH**-rp) receptor mRNA were identified in human kidney, SaOS-2, human osteoblast cells, and rat bone that are produced by alternative splicing of exons coding for the **N-terminal** portion of the receptor. In the S-N3-E2 isoform, the exon coding the signal peptide (S) is spliced to an alternative 3'-acceptor site, producing a product respecting the reading frame, but in which the E1 exon is replaced by 12 amino acids derived from the N3 intron. In the S-E2 isoform, in which the E1 exon is deleted by cassette exclusion, the reading frame is changed, but a truncated receptor may be produced by reinitiation of translation at an overlapping stop/start codon. After transfection of COS and Chinese hamster ovary cells with the originally described S-E1-E2 isoform and the two splice variants, active transcription of **PTH/PTH**-rp receptor mRNA was detected by RT-PCR in all cases. Cell lines transfected with the S-E1-E2 and S-N3-E2 isoforms displayed a 15- to 25-fold and 2- to 3-fold increase, respectively, in cAMP content after stimulation with 2.4 x 10 super(-7) M human **PTH**(1-34), whereas cells transfected with the S-E2 isoform did not respond. **PTH** elicited an increase in intracellular calcium only in cells transfected with the S-E1-E2 isoform. Studies evaluating the surface expression of receptors using anti-human **PTH/PTH**-rp receptor **antibodies** and the ability of transfected cells to bind [super(125)I]**PTH**-rp indicated that the low or absent responses to **PTH** stimulation resulted, at least in part, from low surface expression of the S-N3-E2 and S-E2 isoforms. These studies support the conclusion that exon E1 is extremely important in promoting surface expression of the **PTH/PTH**

Schilling T.
CORPORATE SOURCE: Endocrine Laboratory, Laboratory Group, Im Breitspiel 15,D-69126 Heidelberg, Germany.
SOURCE: Clinica Chimica Acta, (1996), 245/1 (39-59)
CODEN: CCATAR ISSN: 0009-8981
DOCUMENT TYPE: Journal; Article
COUNTRY: Netherlands
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1996:26066917 BIOTECHNO
AB We have developed an immunochemiluminometric assay (ICMA) with two monoclonal **antibodies** for the **N-terminal** sequence of human parathyroid hormone (hPTH). One monoclonal **antibody** (A1-70) was physically adsorbed onto polystyrene beads, the other (B1-70) was labelled with acridinium ester and synthetic hPTH (1-38) was used as standard. This assay has cross-reactions with synthetic hPTH (1-34) and hPTH (1-84) but no cross-reactions with hPTH (4-16), (28-48), (39-84), (44-68), (53-84) and hPTH-rP (1-86). The assay detection limit is 0.4 pmol/l. The normal range is 1.3-12 pmol/l based on 72 normal volunteers. About 91% of study patients (n = 58) with surgically proven primary hyperparathyroidism (1°HPT) had **PTH** values above normal and one of them showed a low normal intact **PTH** value but elevated **PTH** values with use of this assay. After immunoabsorption of plasma samples from patients with secondary hyperparathyroidism (2°HPT) on hemodialysis with polystyrene beads containing **antibodies** against hPTH (39-84), some patients still showed significant amounts of **PTH** in this new ICMA but not intact **PTH**. The data reveal that significant amounts of amino-terminal immunoreactive **PTH** fragments rarely exist in 1°HPT but are present in some patients with 2°HPT. The major advantage of this assay is to measure both amino-terminal **PTH** fragments and intact **PTH** with no interference from carboxy-terminal **PTH** fragments because two anti-**N-terminal** hormone sequence monoclonal **antibodies** are used.

L18 ANSWER 13 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1995:25164106 BIOTECHNO
TITLE: Performance characteristics of different immunoassays for determination of parathyrin (1-84) in human plasma samples
AUTHOR: Withold W.; Schallenberg A.; Reinauer H.
CORPORATE SOURCE: Ist. Klin. Chemie Laboratoriumsdiag., Medizinische Einrichtungen, Heinrich-Heine-Univ. Dusseldorf, Moorenstrasse 5,D-40225 Dusseldorf, Germany.
SOURCE: European Journal of Clinical Chemistry and Clinical Biochemistry, (1995), 33/5 (307-313)
CODEN: EJCBEO ISSN: 0939-4974
DOCUMENT TYPE: Journal; Article
COUNTRY: Germany, Federal Republic of
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1995:25164106 BIOTECHNO
AB The performance characteristics of four radioisotopically and non-radioisotopically labelled two-site immunoassays for the determination of 'intact' parathyrin in plasma samples are reported. Within-run as well as between-assay imprecision was characterized by coefficients of variation usually < 10%. Assessment of the linearity of dilution in plasma samples from patients with severe secondary hyperparathyroidism (obtained from patients with chronic renal failure prior to dialysis) revealed that an assay with **N-terminal** capture **antibodies** showed an increase of the values after dilution ($p < 0.05$) whereas another assay with C-terminal

capture **antibodies** was characterized by a decrease of the values after dilution ($p < 0.05$). Correlation between the data obtained by the four assays and our currently used routine method (N-tact® **PTH** from INCSTAR) revealed correlation coefficients of $r > + 0.96$ and slope values between 0.83 and 1.34. Determination of the analytical recovery of parathyrin (1-84) from two reference materials revealed that the recovery rates were strongly influenced by (a) the assay employed for determination of parathyrin concentrations, (b) the matrix of the diluent and (c) the reference material used. These results as well as systematic differences between the assays we examined (employing plasma samples from unselected nephrological patients) require further efforts towards a more rigorous standardization of 'intact' parathyrin assays.

L18 ANSWER 14 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1995:25213051 BIOTECHNO
TITLE: Parathyroid hormone-related peptide and 8701-BC breast cancer cell growth and invasion in vitro: Evidence for growth-inhibiting and invasion-promoting effects
AUTHOR: Luparello C.; Burtis W.J.; Raue F.; Birch M.A.; Gallagher J.A.
CORPORATE SOURCE: Dipt Biol Cellulare dello Sviluppo, Universita di Palermo, Parco D'Orleans II, Viale delle Scienze,90128 Palermo, Italy.
SOURCE: Molecular and Cellular Endocrinology, (1995), 111/2 (225-232)
CODEN: MCEND6 ISSN: 0303-7207
DOCUMENT TYPE: Journal; Article
COUNTRY: Ireland
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1995:25213051 BIOTECHNO
AB It has been previously reported that 8701-BC cells, derived from a primary carcinoma of the breast, constitutively express parathyroid hormone-related peptide (PTHrP) gene and that **N-terminal** PTHrP immunoreactivity can be found in cell medium. Here we have firstly measured immunoreactive PTHrP in 8701-BC cell medium using **antibodies** raised against midregion and C-terminal fragments, and also demonstrated the expression of **PTH**/PTHrP receptor by 8701-BC cells. Secondly, we have examined the role, if any, elicited by diverse PTHrP domains on 8701-BC cell proliferation, and invasive behaviour in vitro related to production of extracellular proteolytic enzymes. Our data show that PTHrP ¢1-34!, and, to a minor extent, ¢67-86! and ¢107-139!, are anti-mitogenic but 'invadogenic' for 8701-BC cells, and suggest that diverse enzymatic activities may contribute to cell invasion in response to different PTHrP fragments. In light of the present data on a chemoattractive role for PTHrP in vitro, we hypothesize that this protein might intervene in local control of the invasive process in breast carcinoma.

L18 ANSWER 15 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1992:22161863 BIOTECHNO
TITLE: Modified immunoradiometric assay of parathyroid hormone-related protein: Clinical application in the differential diagnosis of hypercalcemia
AUTHOR: Pandian M.R.; Morgan C.H.; Carlton E.; Segre G.V.
CORPORATE SOURCE: Nichols Institute, 26441 Via de Anza,San Juan Capistrano, CA 92675, United States.
SOURCE: Clinical Chemistry, (1992), 38/2 (282-288)
CODEN: CLCHAU ISSN: 0009-9147
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AN 1992:22161863 BIOTECHNO

AB We have developed a sensitive, specific solid-phase immunoradiometric assay (IRMA) of parathyroid hormone-related protein (**PTH**-RP) with use of affinity-purified polyclonal immunoglobulins. **Antibodies** recognizing **PTH**- RP(37-74) are immobilized to a polystyrene bead to 'capture' analytes from the sample; **antibodies** to epitopes within the 1-36 amino acid region of **PTH**- RP are labeled with .sup.1.sup.2.sup.5I. This IRMA recognizes **PTH**-RP(1-74) and **PTH**-RP(1- 86) equivalently, but does not detect **N-terminal** or C-terminal fragments of **PTH**-RP, intact human parathyrin (**PTH**), or fragments of **PTH**. **PTH**-RP is not stable in plasma at 3-5 °C or room temperature, but a mixture of aprotinin (500 kallikrein units/L) and leupeptin (2.5 mg/L) improves **PTH**-RP stability in blood samples. In plasma collected in the presence of these protease inhibitors from normal volunteers and patients with various disorders of calcium metabolism, **PTH**-RP concentrations were above normal (>1.5 pmol/L) in 91% (42 of 46) of patients with hypercalcemia associated with nonhematological malignancy. In plasma from patients with other hypercalcemic conditions (e.g., primary hyperparathyroidism, sarcoidosis, and vitamin D excess), **PTH**-RP was undetectable. Above-normal concentrations of **PTH**-RP and total calcium decreased to normal in a patient with an ovarian cyst adenocarcinoma after surgical removal of the tumor. We conclude that **PTH**-RP is related to and probably the causative agent of hypercalcemia in most patients with cancer, and that measurements of **PTH**-RP are useful in the diagnosis and management of patients with tumor-associated hypercalcemia.

L18 ANSWER 16 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN

ACCESSION NUMBER: 1992:24167605 BIOTECHNO

TITLE: Plasma parathyroid hormone and calcitonin levels, measured by immunoradiometric assay, in very old patients, over 90 years; relation with osteoporosis. Study on 19 cases

AUTHOR: Perietianu D.; Grigorie D.; Zaharescu J.; Saragea M.

CORPORATE SOURCE: Dept. of Endocrinol./Appl. Immunol., 'Sf. Ion' Hospital,Bucharest, Romania.

SOURCE: Romanian Journal of Gerontology and Geriatrics, (1992), 13/- (31-38)
CODEN: RJGGDV ISSN: 0254-2307

DOCUMENT TYPE: Journal; Article

COUNTRY: Romania

LANGUAGE: English

SUMMARY LANGUAGE: English; French; Romanian

AN 1992:24167605 BIOTECHNO

AB In 19 institutionalized elderly patients, over 90 years (x: 92.9), 4M/15F, with normal calcium diet (1.5 g/day) and vit. D aport (500 iu), with sun exposure score 11 from 12, edentated, with reduced height over 10 cm, 10 cases of kyphosis, kyphoscoliosis, all severe, only 2 cases of hip fracture (10.52%), we analysed **PTH** and calcitonin, by an IRMA technique (Medgedix, Belgium), versus a control group of 18 subjects, aged 20-87 (x: 43.87), 5M/13F. The method for **PTH** assay (double **antibody**, I: anti 1-34 **N** (**terminal**, polyclonal obtained from goat, II: anti 44-68, monoclonal, bound by 125-I) allows to measure intact hPTH, in normal range of 5-20 pg/ml. Any value over 40 pg/ml can be considered hyperPTHemia. The assay for calcitonin (oligoclonal system with two monoclonal **antibodies**, uptake and signal, bound by 125-I) allows to identify monomers, polymers but not CT-like proteins, in normal range of 0-15 pg/ml. **PTH**-IRMA in elderly vs. controls is moderately increased but significantly: $p < 0.001$; $t = 3.96$, x: 33.49 vs. 10.19 pg/ml. In 7 cases (36.8%) the **PTH** level overpass 40

pg/ml. The highest value: 86.8 pg/ml. Between M/F there is an unsignificant difference: 30.13 vs. 46.1. CT-IRMA does not differ between groups: 9.74 vs. 10.59 pg/ml. In F vs. M it is slightly but unsignificantly decreased: 9.3 vs. 11.42 pg/ml. There is not a significant correlation between the severity of osteoporosis and the level of **PTH** over 40 pg/ml (x.sup.2 = 0.05). The normal level of vit. D, infer from diet and sun exposure, correlated with the normal level of calcitonin, but correlated with the low prevalence of long bone fractures suggest that the increase of **PTH** level in elderly could be a protective antiosteoporosis factor.

L18 ANSWER 17 OF 29 LIFESCI COPYRIGHT 2005 CSA on STN
ACCESSION NUMBER: 93:58348 LIFESCI
TITLE: Hyperphosphatemia in multiple myeloma due to a phosphate-binding immunoglobulin.
AUTHOR: Mandry, J.M.; Posner, M.R.; Tucci, J.R.; Eil, C.
CORPORATE SOURCE: Dep. Med., Div. Endocrinol., Roger Williams Gen. Hosp., 825 Chalkstone Ave., Providence, RI 02908, USA
SOURCE: CANCER., (1991) vol. 68, no. 5, pp. 1092-1094.
DOCUMENT TYPE: Journal
FILE SEGMENT: T; F
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Hyperphosphatemia (HP) is usually seen in patients with hypoparathyroidism, renal failure, and tumor lysis. The authors described a patient with HP due to a phosphate-binding immunoglobulin (Ig). An 86-year-old woman had serum phosphate levels as high as 4.75 mmol/l, (normal 0.77 to 1.45 mmol/l). Serum ionized calcium, blood urea nitrogen (BUN), creatinine, and **N-terminal** parathyroid hormone (**PTH**) levels were normal, but serum 1,25-dihydroxyvitamin D level was subnormal at less than 12 pmol/l (normal, 36 to 146 pmol/l). Serum total protein was elevated at 105 g/l (normal, 60 to 80 g/l), and additional studies confirmed a diagnosis of immunoglobulin G (IgG) multiple myeloma. The studies of the authors document phosphate binding by an IgG paraprotein and suggest that in this setting HP may may be of physiologic significance as evidenced by depressed serum levels of 1,25-dihydroxyvitamin D.

L18 ANSWER 18 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1991:21314801 BIOTECHNO
TITLE: Ontogeny of parathyroid hormone-related protein in the ovine parathyroid gland
AUTHOR: MacIsaac R.J.; Caple I.W.; Danks J.A.; Diefenbach-Jagger H.; Grill V.; Moseley J.M.; Southby J.; Martin T.J.
CORPORATE SOURCE: St. Vincents Inst. of Med. Res,Fitzroy, Vic. 3065, Australia.
SOURCE: Endocrinology, (1991), 129/2 (757-764)
CODEN: ENDOAO ISSN: 0013-7227
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1991:21314801 BIOTECHNO
AB **PTH**-related protein (PTHrP) has been implicated in calcium regulation during fetal life. In this study the ontogeny of PTHrP was examined in ovine parathyroid glands. Immunohistochemical techniques, Western blot analysis, and a RIA with antisera raised against synthetic fragments of human (h) PTHrP (i.e. 1-34, 1-40, 50-69, and 107-141) were used to detect the presence of immunoreactive PTHrP in parathyroid glands from fetal and neonatal lambs and maternal ewes. Positive immunostaining for PTHrP was observed in fetal (from 116 days of gestation) and lamb (up to 180 days post birth) but not maternal parathyroid glands with the

PTHrP(50-69) antiserum. Fetal and lamb parathyroid glands consisted entirely of one cell type in which PTHrP immunoreactivity to PTHrP(50-69) antiserum was found. In contrast, immunoreactivity to PTHrP could not be detected in sections of fetal, lamb, or maternal parathyroid glands with antisera raised against PTHrP(1-34) or PTHrP(107-141). However, PTHrP immunoreactivity in urea/ acid extracts of newborn lamb parathyroid glands could be detected by Western blot analysis and RIA with antisera raised against the **N-terminal** portion of PTHrP.
Western blot analysis with the PTHrP(1-34) antisera revealed that urea/acid extracts of newborn lamb parathyroid glands contained a substance with a mol wt of 14.4K, which corresponded in size to that of hPTHrP(1-84). Newborn lamb parathyroid glands contained 0.35 ng PTHrP/μg extract, whereas maternal parathyroid glands contained only 0.035 ng PTHrP/μg extract when tested in a RIA employing recombinant hPTHrP(1-84) as standard and an **antibody** raised against hPTHrP(1-40). The detection of immunoreactive PTHrP in the developing ovine parathyroid gland provides further evidence to support the suggestion that PTHrP produced in the parathyroid gland is involved in the normal hormonal regulation of calcium metabolism in the mammalian fetus and neonate.

L18 ANSWER 19 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1991:21310522 BIOTECHNO
TITLE: Parathyroid hormone-related protein: Biochemistry and molecular biology
AUTHOR: Martin T.J.; Moseley J.M.; Gillespie M.T.
CORPORATE SOURCE: Department of Medicine, University of Melbourne, and St. Vincent's Institute of Medical Research, St. Vincent's Hospital, Fitzroy, Vic. 3065, Australia.
SOURCE: Critical Reviews in Biochemistry and Molecular Biology, (1991), 26/3-4 (377-395)
CODEN: CRBBEJ ISSN: 1040-9238
DOCUMENT TYPE: Journal; General Review
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1991:21310522 BIOTECHNO
AB This article critically reviews the current state of knowledge regarding the recently identified and cloned novel hormone parathyroid hormone-related protein (PTHrP). PTHrP is produced by tumors associated with the syndrome of humoral hypercalcemia of malignancy giving rise to the parathyroid hormone (**PTH**)-like symptoms characteristic of the syndrome. Areas that will be reviewed include identification, purification and cloning, localization, actions, and significance of PTHrP in cancers and normal physiology. The structure and regulation of the PTHrP gene that may be ancestrally related to the **PTH** gene will also be discussed. Studies in vivo and in vitro with synthetic and recombinant PTHrP sequences and **antibodies** developed against them have established that the **PTH**-like actions of PTHrP are mediated via the **N-terminal** sequences, which show some limited sequence homology with **PTH**. Evidence for **PTH** and non-**PTH**-like actions of PTHrP in normal physiology, which implicate a role for PTHrP in fetal and neonatal development, is also presented.

L18 ANSWER 20 OF 29 LIFESCI COPYRIGHT 2005 CSA on STN
ACCESSION NUMBER: 93:122370 LIFESCI
TITLE: Altered differentiation of limb bud cells by transforming growth factors- beta isolated from bone matrix and from platelets.
AUTHOR: Schoenfeld, H.-J.; Poeschl, B.; Wessner, B.; Kistler, A.
CORPORATE SOURCE: Central Res. Units, F. Hoffmann-La Roche Ltd., 4002 Basle, Switzerland

SOURCE: BONE MIN., (1991) vol. 13, no. 3, pp. 171-189.
DOCUMENT TYPE: Journal
FILE SEGMENT: T; M; B
LANGUAGE: English
SUMMARY LANGUAGE: English

AB A crude extract of demineralized bone matrix caused an altered differentiation of limb bud cells which was seen within 5 days in culture. Using this bioassay system we purified two factors to homogeneity and found that according to their **N-terminal** sequences they corresponded to TGF- beta sub(1) and TGF- beta sub(2) isolated from platelets. Biochemical analyses and biological studies (molecular mass determination, inactivation by reducing agents and proteases, **antibody** neutralization, competitive binding to TGF- beta receptors and influence on protein expression) provided additional evidence that the two proteins isolated from demineralized bone matrix were apparently identical to TGF- beta sub(1) and TGF- beta sub(2). Proteoglycan content, alkaline phosphatase activity and response of the cells to **PTH** stimulated adenylate cyclase were quantitatively changed by the factors. Culturing limb bud cells on polycarbonate membranes resulted in a rapid and extensive growth and differentiation of the cells to palpable tissue pieces. Relative to controls distinct cell and tissue morphology was observed macroscopically and in histological sections of these tissue pieces. (DBO)

L18 ANSWER 21 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1991:21146931 BIOTECHNO
TITLE: Production and characterisation of monoclonal **antibodies** to parathyroid hormone (1-34)
AUTHOR: Logue F.C.; Perry B.; Biggart E.M.; Chapman R.S.; Beastall G.H.
CORPORATE SOURCE: Institute of Biochemistry, Royal Infirmary,Glasgow G4 OSF, United Kingdom.
SOURCE: Journal of Immunological Methods, (1991), 137/2 (159-166)
CODEN: JIMMBG ISSN: 0022-1759
DOCUMENT TYPE: Journal; Article
COUNTRY: Netherlands
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1991:21146931 BIOTECHNO

AB Monoclonal **antibodies** to the biologically active **N terminal** region of parathyroid hormone (**PTH**) suitable for use in the measurement of circulating **PTH** concentrations have proved difficult to produce. In this study, no serum **PTH antibody** titres could be detected in mice using synthetic human **PTH** (1-34) (free or coupled to albumin) or **PTH** (1-10) (coupled to keyhole limpet haemocyanin) as immunogen. A consistent response to **PTH** (1-34) peptide was obtained in DA rats. We have produced five monoclonal **antibodies** to **PTH** (1-34) derived from the fusion of DA rat spleen cells and the mouse myeloma line X63 Ag.8.653. Bulk production of the **antibodies** was achieved using congenitally athymic mice for ascites production. **Antibody** assessment studies revealed the **antibodies** to be sensitive to the oxidation state of the methionine residues in **PTH** (1-34). Two of the **antibodies**, 3B3 and 6E3, were shown to be of potential use in measuring circulating **PTH** (1-84) when used in combination with available **antibodies** to C terminal **PTH** . A third **antibody**, 4G3, which failed to recognise **PTH** (1-84) when used in combination with 3B3, formed the basis of a specific assay for **PTH** (1-34).

L18 ANSWER 22 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1988:18241977 BIOTECHNO

TITLE: Clinical applicability of an amino-terminal radioimmunoassay for determination of parathyroid hormone
AUTHOR: Mollerup C.L.; Bruun E.; Hesselfeldt-Nielsen J.; Hummer L.
CORPORATE SOURCE: Department of Endocrine Surgery, Rigshospitalet, Copenhagen, Denmark.
SOURCE: Acta Chirurgica Scandinavica, (1988), 154/7-8 (419-423)
CODEN: ACHSA3 ISSN: 0001-5482
DOCUMENT TYPE: Journal; Article
COUNTRY: Sweden
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1988:18241977 BIOTECHNO
AB With a radioimmunoassay using hPTH 1-34 for **antibody** production, for radioiodination and as a standard, hPTH 1-34 was detectable (detection limit 40 pg/ml) preoperatively in peripheral blood in 14 of 29 patients with hyperparathyroidism, but in no controls. In all patients with parathyroid adenoma and detectable hPTH 1-34 preoperatively, the values fell after parathyroid surgery. Contrastingly, three of four patients with diffuse parathyroid hyperplasia and two of three with normal parathyroid glands showed a rise in hPTH 1-34 postoperatively, which was concomitant with very low serum calcium levels. In studies of hPTH 1-34 in central venous blood (3 patients), levels were detectable in all samples, but not in simultaneously drawn peripheral blood. Values for hPTH 1-34 in central blood correlated to **PTH** determined from a bovine assay, but the peripheral samples showed no correlation. The low levels of circulating **N-terminal** immunoreactivity in peripheral blood make this assay inapplicable for routine diagnostic purposes. These low levels are due not only to low secretion rates, but also to rapid peripheral metabolization.

L18 ANSWER 23 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1987:18041974 BIOTECHNO
TITLE: Measurement of intact human parathyrin by an extracting two-site immunoradiometric assay
AUTHOR: Blind E.; Schmidt-Gayk H.; Armbruster F.P.; Stadler A.
CORPORATE SOURCE: Klinisches Laboratorium, Chirurgische Universitatsklinik, D-6900 Heidelberg, Germany.
SOURCE: Clinical Chemistry, (1987), 33/8 (1376-1381)
CODEN: CLCHAU ISSN: 0009-9147
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1987:18041974 BIOTECHNO
AB This is an immunoradiometric assay of intact human parathyrin, hPTH(1-84). One **antibody**, directed against the **N-terminal** part of the hormone, was produced in goats and conjugated covalently to cellulose particles. hPTH(1-84) and the **N-terminal** fragments were extracted from EDTA-treated plasma by these particles and thus concentrated. Another **antibody**, against synthetic hPTH(53-84), was raised in rabbits; this bound to the C-terminal part of the hormone. The final step was labeling the second free binding site of this **antibody** with .sup.1.sup.2.sup.5I-labeled Tyr.sup.5.sup.2-hPTH(53-84) and measuring the bound radioactivity. This assay can detect intact **PTH** in concentrations as low as 0.6 pmol/L (1.2 x 10.sup.-.sup.1.sup.6 mol per tube). The assay did not cross react with hPTH(1-34), hPTH(1-44), hPTH(28-48), hPTH(39-84), hPTH(44-68), or hPTH(53-84) in concentrations up to 6400 pmol/L. In 60 normal subjects, hPTH(1-84) concentrations

ranged from 1.9 to 6.8 pmol/L; in 32 patients with primary hyperparathyroidism, from 7.0 to 80 pmol/L. The hormone was not detected in four patients with hypoparathyroidism.

L18 ANSWER 24 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1985:15230526 BIOTECHNO
TITLE: Daily **PTH** secretion in adult subjects
SECREZIONE GIORNALIERA DI **PTH** IN SOGGETTI ADULTI
AUTHOR: Mauri R.; Resentini M.; Lissoni P.; et al.
CORPORATE SOURCE: Centro Auxologico Italiano, Divisione di Endocrinologia, Piancavallo, Italy.
SOURCE: Minerva Medica, (1985), 76/26-27 (1271-1273)
CODEN: MIMEAO
DOCUMENT TYPE: Journal; Article
COUNTRY: Italy
LANGUAGE: Italian
SUMMARY LANGUAGE: English
AN 1985:15230526 BIOTECHNO
AB Data reported in the literature on the existence of a circadian rhythm in **PTH** secretion are contradictory. In order to assess whether haematic **PTH** levels vary over a 24 hour period, the plasma levels of the hormone were evaluated at 6 different times during the day (12, 19, 24, 2, 4, 6 hours) in a group of 10 healthy adults (5 males, 5 females), aged from 24.8 to 48.7 years. **PTH** values were determined by the double **antibody** radioimmunological method using commercially available kits (**PTH**-K Sorin-Saluggia), whose antiserum reacts with the C terminal fraction of the hormone. No statistically significant differences were observed, either between the sexes or among the samples collected during the 24 hour period. The results therefore seem to preclude the existence of a circadian rhythm in **PTH** secretion. However, further studies and more data - based on RIA methods, whose antiserum reacts with the **N terminal** of the hormone - would be necessary to preclude the existence of rapid circadian variations in **PTH** over the 24 hour period.

L18 ANSWER 25 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
DUPLICATE
ACCESSION NUMBER: 1983:14204302 BIOTECHNO
TITLE: Estimation of biologically active intact parathyroid hormone in normal and hyperparathyroid sera by sequential **N-terminal** immunoextraction and midregion radioimmunoassay
AUTHOR: Lindall A.W.; Elting J.; Ells J.; Roos B.A.
CORPORATE SOURCE: Immuno Nuclear Corporation, Stillwater, MN 55082, United States.
SOURCE: Journal of Clinical Endocrinology and Metabolism, (1983), 57/5 (1007-1014)
CODEN: JCEMAZ
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
AN 1983:14204302 BIOTECHNO
AB We report a two-step immunochemical method for estimating serum intact **PTH**, as defined by immunochemical methods, and its validation by a newly developed osteosarcoma cell adenyl cyclase stimulation assay for **PTH** bioactivity. The first step involves extraction and concentration of serum **PTH** moieties with solid phase amino-terminal **PTH antibodies**; in the second step, the initial **PTH** immunoextract is analyzed with a sensitive midregion immunoassay. Intact **PTH** can thus be detected in virtually all normal subjects. Intact **PTH** levels in our group of primary hyperparathyroid persons average nearly 20 times higher than

normal and do not overlap the normal range. Intact **PTH** is also elevated in chronic renal disease, but less dramatically than in primary hyperparathyroidism. Since total **PTH** immunoreactivity (intact plus fragments) is much higher in renal disease patients than in persons with primary hyperparathyroidism, serum intact **PTH** in renal disease apparently comprises a much smaller fraction of total circulating **PTH** immunoreactivity than in primary hyperparathyroidism. The finding that intact **PTH** accounts for a large portion of total circulating **PTH** immunoreactivity in primary hyperparathyroidism is contrary to published reports by us and others. Some of the possible reasons for the differences between our present results and previous reports are examined.

L18 ANSWER 26 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1982:13254064 BIOTECHNO
TITLE: Parathyroid hormone assay
AUTHOR: Chih Kao P.
CORPORATE SOURCE: Dep. Lab. Med., Mayo Clin., Rochester, MN, United States.
SOURCE: Mayo Clinic Proceedings, (1982), 57/9 (596-597)
CODEN: MACPAJ
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
AN 1982:13254064 BIOTECHNO
AB Antiserum GP-235 recognizes intact whole-molecule **PTH** and C-terminal fragments of 44-68 and 53-84 amino acid sequences but does not recognize the **N-terminal** 1-34 amino acid sequence. A radioimmunoassay was developed with this antiserum, and 118 normal subjects of both sexes from 20 to 55 years of age were studied. The serum **PTH** concentrations in all of these subjects were less than 70 μleq/ml, which is our upper limit of normal. The radioimmunoassay developed with this antiserum can differentiate normal subjects from patients with primary hyperparathyroidism, hypoparathyroidism, chronic renal failure, or hypercalcemia caused by malignancy.

L18 ANSWER 27 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
DUPLICATE
ACCESSION NUMBER: 1981:13144962 BIOTECHNO
TITLE: 1-34 Human parathyroid hormone radioimmunoassay: Properties of antiserum against synthetic 1-34 human parathyroid hormone and its clinical application
AUTHOR: Shiraki M.; Kawada N.; Akiguchi I.; et al.
CORPORATE SOURCE: Dep. Endocrinol. Metab., Tokyo Metrop. Geriatr. Hosp., Itabashiku, Tokyo, Japan.
SOURCE: Endocrinologia Japonica, (1981), 28/2 (239-244)
CODEN: ECJPAE
DOCUMENT TYPE: Journal; Article
COUNTRY: Japan
LANGUAGE: English
AN 1981:13144962 BIOTECHNO
AB **Antibody** against synthetic 1-34 human **PTH** synthesized by Niall et al. (1974), was developed in rabbits. Synthetic 1-34 hPTH was found to be a good immunogen for rabbit. The relative importance of various structural parts of 1-34 hPTH molecule with regard to immunological specificity was determined by reference to inhibition of specific binding of .sup.1.sup.2.sup.5I-1-34 hPTH to the **antibody** by analogues of 1-34 hPTH (NLeu.sup.8-NLeu.sup.1.sup.8 1-34 hPTH, NLeu.sup.8-NLeu.sup.1.sup.8-Tyr.sup.3.sup.4hPTH) and by 1-34 bPTH. The immunological recognition site in 1-34 hPTH molecule was found to be located around the 8 to 18 amino acid sequence, because the binding affinity to the **antibody** of this analogue (NLeu.sup.8-NLeu.sup.1.sup.81-34 hPTH) was less than that of the native hormone in

the **antibody**. Furthermore, other immunological recognition sites were located in the C- and **N-terminal** regions of this molecule, as reported by Segre et al. (1976) and Visser et al. (1979). This antiserum could measure only 1-34 hPTH molecle in serum, since it did not crossreact with partially purified 1-84 hPTH. In order to evaluate the advantage of 1-34 hPTH radio-immunoassay (RIA) in the diagnosis of parathyroid dysfunction, serum **PTH** levels in various diseases were measured by both 1-34 hPTH RIA and 1-84 **PTH** RIA and the values obtained by these assays were compared. There was a good correlation between the values obtained by 1-34 hPTH RIA and those by 1-84 **PTH** RIA. However, in patients with chronic renal failure, the incidence of cases with high serum **PTH** level was 90% when measured by 1-84 **PTH** RIA while it was 39% when measured by 1-34 hPTH RIA. Serum **PTH** levels in primary hyperparathyroidism were abnormally high and those in hypoparathyroidism were low in both assays. Some patients with senile osteoporosis had a high serum **PTH** level. The incidences of cases with a high serum **PTH** level in this disease were equal in both assays. In conclusion, these two site specific RIAs (1-34 **PTH** RIA and 1-84 **PTH** RIA) were useful in the evaluation of **PTH** secretion and/or metabolism.

L18 ANSWER 28 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1979:10165597 BIOTECHNO
TITLE: A radioimmunoassay for plasma parathyroid hormone (**PTH**) using **N-terminal** **PTH** antiserum
AUTHOR: Kayamori R.; Yamada Y.; Ito S.; et al.
CORPORATE SOURCE: Coll. Bio-Med. Technol., Niigata Univ., Niigata, Japan.
SOURCE: Folia Endocrinologica Japonica, (1979), 55/11 (1372-1383)
CODEN: NNGZAZ
DOCUMENT TYPE: Journal; Article
COUNTRY: Japan
LANGUAGE: Japanese
SUMMARY LANGUAGE: English
AN 1979:10165597 BIOTECHNO
AB In order to investigate plasma bioactive **PTH**, we tried to assay the **N-terminal** portion of **PTH** by RIA. The antiserum to **PTH** was prepared by immunizing rabbits with a bovine 1-34 **PTH** conjugate BSA. A preparation of labeled **PTH** was radioiodinated by the chloramine-T or lactoperoxidase method. Labeled **PTH** was purified by means of adsorption by Quso G-32 powder or a sephadex G-50. Separation of the free and bound labeled hormone was performed by the dextran-coated charcoal method. The assay was carried out as follows: 0.2 ml diluted buffer (0.05M, pH 8.6, veronal buffer), 0.1 ml standard **PTH** or sample to be tested, and 0.1 ml anti-**PTH** serum were mixed. After the first incubation at 4°C for 4 days, 0.1 ml labeled **PTH** were added. After a second incubation at 4°C for 12 hours, the assay tubes were centrifuged at 2,000 rpm for 30 min and the precipitates were counted. Various hypothalamic, pituitary and thyroid hormones did not interfere with the RIA for **PTH**. A dose response curve was obtained in a range from 100 pg to 5,000 pg per ml of standard **PTH** in this assay system. The serum immunoreactive **PTH** in healthy subjects showed values less than 290 pg per ml.

L18 ANSWER 29 OF 29 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1979:10212687 BIOTECHNO
TITLE: Development of sequence specific radioimmunoassay of human parathyroid hormone and its use in the diagnosis of hyperparathyroidism

AUTHOR: Gautvik K.M.; Teig V.; Halvorsen J.F.; et al.
CORPORATE SOURCE: Inst. Surg. Res., Rikshosp., Univ. Oslo, Norway.
SOURCE: Scandinavian Journal of Clinical and Laboratory Investigation, (1979), 39/5 (469-478)
CODEN: SJCLAY
DOCUMENT TYPE: Journal; Article
COUNTRY: Norway
LANGUAGE: English
AN 1979:10212687 BIOTECHNO
AB Two antisera which were raised against bovine parathyroid hormone (bPTH), and which cross-reacted with the human hormone, have been characterized. The antisera which originated from rooster and guinea-pig, were found to contain several populations of **antibodies** directed against both **N-terminal** and C-terminal sequences of the hormone. However, at proper dilutions the rooster antiserum did not bind the **N-terminal** fragment nor could this fragment displace the ¢.sup.1.sup.2.sup.5I! bPTH (1-84 amino acid residue) from binding to the antiserum. Furthermore, preincubation experiments with excess **N-terminal** fragment showed only a negligible reduction in maximal binding of the iodinated intact hormone using the rooster antiserum. In contrast, the guinea-pig antiserum reacted equally well with the **N-terminal** fragment and the intact hormone, and preincubation with this fragment reduced the binding of the ¢.sup.1.sup.2.sup.5I!bPTH (1-84 amino acid residues) by 75%. Gel filtration of hyperparathyroid serum on Bio-Gel P-60 showed immunoreactive material which was measured with both antisera, eluting at a position similar to the intact hormone. However, in the C-terminal specific, but not in the **N-terminal** specific radioimmunoassay the major component eluted together with or somewhat earlier than the **N-terminal** bPTH fragment (1-34 amino acid residue), and this peak represented more than 90% of total immunoreactive **PTH** (iPTH) in serum. This major iPTH component must therefore represent fragment(s) with intact carboxy-terminal sequences. The **N-terminal** specific radioimmunoassay was unable to measure iPTH in about 80-90% of healthy individuals while the C-terminal specific assay detected iPTH in about 88% of these sera (equal to or above 0.1 μg/l). Similarly, the **N-terminal** specific antiserum measured consistently lower serum iPTH concentrations in patients with primary hyperparathyroidism. In thirty-four out of forty-one patients with surgically verified primary hyperparathyroidism, serum iPTH concentrations equal to or above 0.60 μg/l were demonstrated using the C-terminal, specific radioimmunoassay.